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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re U.S. Patent Application of:

Joseph A. SORGE et al.

U.S. Application No.: 10/734,563

Filing Date: 12 December 2003

Group Art Unit: 1652

Examiner: R. HUTSON

Confirmation Number: 2401

Title: DNA POLYMERASE COMPOSITIONS FOR QUANTITATIVE PCR AND METHODS THEREOF

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Sir:

REPLY BRIEF UNDER BOARD RULE 37 C.F.R. § 41.41

Appellants filed an Appeal Brief on 30 October 2008. In response to the Examiner's Answer mailed 8 July 2009, and pursuant to Board Rule 41.41, Appellants present this Reply Brief. This Reply Brief is due by 8 September 2009 and is timely filed.

ARGUMENT

A. The Examiner's Interpretation of the Claims as Providing No Structure Beyond the Recited Mutations Is Erroneous

The central issue on appeal is one of claim interpretation. Claim 1 is directed to a mutant Archaeal DNA polymerase comprising: at least one amino acid mutation in the exo I motif, and an amino acid mutation at V93 in an amino acid sequence selected from one of SEQ ID NOs. 83-108, where said mutant Archaeal DNA polymerase is deficient in 3' to 5' exonuclease activity. Claims 2-7 are similarly directed to mutant Archaeal DNA polymerases with an amino acid mutation at V93 in an amino acid sequence selected from one of SEQ ID NOs. 83-108 and deficient in 3' to 5' exonuclease activity but further recite at least one amino acid mutation in the exo II motif (claim 2), the exo III motif (claim 3), each of the exo I and exo III motifs (claim 4), each of the exo II and exo III motifs (claim 5), each of the exo I and exo II motifs (claim 6), and each of the exo I, exo II, and exo III (claim 7). There is no dispute that the claims are directed to a mutant Archaeal DNA polymerase. *See* Examiner's Answer at page 23 ("[A]ppellants claim 1 is clearly drawn to a 'mutant Archaeal DNA polymerase' . . . .").

But the Examiner interprets the claimed mutant polymerases as lacking any structure except for the structure associated with the recited mutations. Specifically, the Examiner argues that the "rejected claims are interpreted as not requiring any structure beyond that of the specified mutation positions only." Examiner's Answer at page 4, lines 10-11; *see also*, Examiner's Answer at page 6, lines 16-19; page 13, lines 17-20; page 17, lines 12-14; and page 19, lines 13-15. Similarly, the Examiner asserts that

> appellants [*sic*, appellants'] claim 1 is drawn to a mutant DNA polymerase in which the only specified structural limitations are in regard to mutation positions (i.e. at least one amino acid mutation in the exol motif and an amino acid mutation at V93). Outside of the

> structural limitations associated with each of the required two "at least one amino acid mutation" 's [*sic*], the claimed DNA polymerase has no structural limitations. It is further noted that claims 2-7 are interpreted analogously as claim 1, as discussed above, however, with respect to the exoII and exoIII motifs and combinations of the exoI, exoII and exoIII motifs.

Examiner's Answer at page 13, lines 3-10.

Appellants' response is that the Examiner's interpretation is erroneous and ignores structural elements of the claimed subject matter. As argued in the Appeal Brief, the claims recite that the mutant Archaeal DNA polymerase comprises the recited mutations in an amino acid sequence selected from one of SEQ ID NOs. 83-108, or in the case of the elected invention, SEQ ID NO. 89. Appeal Brief at pages 21-22. The amino acid sequences represented by SEQ ID NOs. 83-108 correspond to amino acid sequences of known, wild type Archaeal DNA polymerases and, thus, provide structural elements that the Examiner asserts are missing from the claims.

According to the Examiner, "[t]he reference to SEQ ID NOs. 83-108 is not interpreted as relevant beyond providing a reference to 'V93' . . . ." Examiner's Answer at page 24, lines 11-12. Appellant's response is that the wild type Archaeal DNA polymerase sequences (i.e., SEQ ID NOs. 83-108) provide more than just a reference to V93. They provide a starting point for one of skill in the art to use the sequences to make the claimed mutant polymerases.

The Examiner in *Ex parte Anderson*, Appeal No. 2005-0908 (unpublished opinion)[1] took a similar position as the Examiner does here by arguing that a claim[2] directed to a modified cellulose enzyme comprising a substitution at position 119 of SEQ ID NO:5 broadly "reads on any structure that is not necessarily homologous with SEQ ID NO: 5." *Id.* at 5. The Board rejected this argument and reversed the Examiner's written description rejection, noting that "the claim requires that the skilled practitioner start with a cellulose having the sequence of SEQ ID NO:5." *Id.*

Similarly here, the amino acid sequences of the wild type Archaeal DNA polymerases recited in the claims were known as of Appellants' filing date and provide a starting point for one of skill in the art. Accordingly, using those wild type sequences, one of skill in the art could readily ascertain the mutant DNA polymerases covered by the claims. Thus, the references in the claims to the wild type Archaeal DNA polymerases (i.e., SEQ ID NOs. 83-108) are relevant for more than just providing a reference to V93 and cannot be ignored in interpreting the proper scope of the claimed subject matter.

At pages 19-20 of the Examiner's Answer, the Examiner discusses an after-final amendment submitted by Appellants on 28 April 2008 that changed claim 1 from "An Archaeal DNA polymerase comprising an amino acid sequence selected from SEQ ID NOs. 83-108 and

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1 A copy of *Ex parte Anderson* is attached to this Reply Brief.

2 The claim at issue in *Anderson* recited :

> 204. A modified cellulase, comprising a substitution of the amino acid at position 119 with H in the amino acid of SEQ ID NO: 5, wherein each position is numbered according to the amino acid sequence of the cellulase of SEQ ID NO: 1 and the modified cellulase has endoglucanase activity.

further comprising at least one amino acid mutation in exoI motif and another amino acid mutation at V93 . . ." to "An Archaeal DNA polymerase comprising at least one amino acid mutation in the exoI motif and an amino acid mutation at V93 in an amino acid sequence selected from one of SEQ ID NOs. 83-108 . . . ." Examiner's Answer at page 19, line 16 to page 20, line 14. According to the Examiner, [t]his amendment appears to change the reference to SEQ ID NOs. 83-108 from that which the Archaeal DNA polymerase comprises to that which is a reference for the amino acid mutation positions." Examiner's Answer at page 20, lines 11-13. In addition, the Examiner asserts that "Appellants have not commented as to this amendment regarding the breadth of the claim." Examiner's Answer at page 20, lines 13-14. Appellants' response is that the amendment was made to further clarify the scope of the claimed subject matter. Specifically, the amendment makes clear that the mutant Archaeal DNA polymerase comprises the recited mutations in an amino acid sequence selected from one of SEQ ID NOs. 83-108. This should have been clear from Appellants' statements in the 30 April 2008 Amendment After Final. For example, Appellants state that "claims 1-7 are directed to an Archaeal DNA polymerase comprising an amino acid mutation at V93 and at least one mutation in the recited exonuclease motifs in an amino acid sequence selected from one of SEQ ID NOs. 83-108." Amendment After Final Rejection Under 37 C.F.R. § 1.116 dated 30 April 2008 at page 10; *see also* page 11, lines 13-17.

Although it is clear that the Examiner improperly ignores structural elements in the claims (i.e., the reference to the sequences represented by SEQ ID NOs. 83-108), it is not entirely clear how the Examiner arrives at his conclusions that outside of the recited mutations, "the claimed DNA polymerase has no structural limitations" and that "[t]he reference to SEQ ID NOs. 83-108 is not interpreted as relevant beyond providing a reference to 'V93' . . . ."

Previously, the Examiner argued that the term "at least one mutation . . ." in claims 1-7 opened the claimed genus is such a manner as to effectively eliminate the other recited characteristics in the claims. Appellants addressed this erroneous claim construction in the Appeal Brief. *See* Appeal Brief at pages 22-24. Now, the Examiner appears to have abandoned the argument about the term "at least one mutation" effectively eliminating the other recited characteristics of the claims and instead argues:

> By virtue of appellants [*sic*, appellants'] claims requiring that the Archaeal DNA polymerase be deficient in 3'-5' exonuclease activity, the claimed polymerase is no longer an Archaeal DNA polymerase, on the basis that as submitted by appellants, Archaeal DNA polymerases have a 3'-5' exonuclease activity. Outside of the structural limitations associated with each of the required two "at least one amino acid mutation" 's [*sic*], the claimed DNA polymerase has no structural limitation.

Examiner's Answer, page 20, line 15 to page 21, line 7.

Appellants' response is that a mutant Archaeal DNA polymerase that is deficient in 3'-5' exonuclease activity is still an Archaeal DNA polymerase, albeit a mutant Archaeal DNA polymerase. The fact that an Archaeal DNA polymerase may be mutated to reduce or abolish its 3'-5' exonuclease activity does not mean that one of skill in the art would no longer recognize the mutated polymerase as a mutant Archaeal DNA polymerase. The Examiner certainly has not presented any evidence supporting such an argument.

Furthermore, as discussed in the specification, the term deficient in 3'-5' exonuclease activity means that the mutant DNA polymerase has deficient 3'-5' exonuclease relative to a parental enzyme. It does not require the mutant Archaeal DNA polymerase to have no 3'-5' exonuclease activity. Specifically, the specification defines the term as follows:

> As used herein, "3' to 5' exonuclease deficient" or "3' to 5' exo-" refers to an enzyme that substantially lacks the ability to remove

> incorporated nucleotides from the 3' end of a DNA polymer. DNA polymerase exonuclease activities, such as the 3' to 5' exonuclease activity exemplified by members of the Family B polymerases, can be lost through mutation, yielding an exonuclease-deficient polymerase. As used herein, a DNA polymerase that is deficient in 3' to 5' exonuclease activity substantially lacks 3' to 5' exonuclease activity. "Substantially lacks" encompasses a complete lack of activity, for example, 0.03%, 0.05%, 0.1%, 1%, 5%, 10%, 20% or even up to 50% of the exonuclease activity relative to the parental enzyme. Methods used to generate and characterize 3'-5' exonuclease DNA polymerases including the D141A and E143A mutations as well as other mutations that reduce or eliminate 3'-5' exonuclease activity are disclosed in the pending U.S. patent application Ser. No. 09/698,341 (Sorge et al; filed Oct. 27, 2000). Additional mutations that reduce or eliminate 3' to 5' exonuclease activity are known in the art and contemplated herein.

Specification at page 13.

There is no evidence in the record to support the Examiner's argument that a mutant Archaeal DNA polymerase is no longer an Archaeal DNA polymerase by virtue of its being deficient in 3'-5' exonuclease activity. Accordingly, it is clear error for the Examiner to ignore structural elements recited in the claim based on the fact that the claims recite that the mutant Archaeal DNA polymerase is deficient in 3'-5' exonuclease activity.

The Examiner further agues that the claimed mutant Archaeal DNA polymerase "is not subject to any of the structural limitations of an 'Archaeal DNA polymerase', because it is mutated such that it is no longer an 'Archaeal DNA polymerase'." Examiner's Answer at page 10, line 21 to page 11, line 4 and page 23, line 21 to page 24, line 1.

Appellants' response is that a mutant protein is typically described by reference to a wild type or other reference sequence. Those skilled in the art understand that the wild type or other reference sequence from which the mutant protein is derived provides important structural information about the mutant protein. Thus, one of skill in the art would understand that a mutant Archaeal DNA polymerase is an Archaeal DNA polymerase that has been mutated at

certain amino acid positions. *See e.g.*, Figure 6B (providing "amino acid sequence of example mutant Archaeal DNA polymerases according to one embodiment of the invention."). As such, a mutant Archaeal DNA polymerase is a mutant version of an Archaeal DNA polymerase and, except for those changes introduced by one or mutations, one of skill in the art would expect the mutant Archaeal DNA polymerase to retain the other structural elements of the Archaeal DNA polymerase from which it was derived. Thus, the Examiner's argument that a mutant Archaeal DNA polymerase is not subject to the structural elements of an Archaeal DNA polymerase because it is no longer an Archaeal DNA polymerase is contrary to the state of the art and finds no support in the record.

B. Predictability in the Art

The Examiner argues that the art is unpredictable because 9 of the 25 sequences recited in the claims (i.e., SEQ ID NOs. 83-108) do not have a valine ("V") at amino acid position 93. Examiner's Answer at page 25. Appellants' response is that the lack of a valine at residue 93 in certain of the sequences recited in the claims does not support a finding that the art is unpredictable. The sequences in question either have a valine at position 93 or a valine at a position corresponding to V93—a very predictable result. See Appendix 12 to Examiner's Answer. For sequences that do not have a valine at position 93, one of skill in the art would understand "an amino acid mutation at V93" to mean an amino acid mutation at a position corresponding to V93. Otherwise, the term does not make sense and would exclude from the claims embodiments disclosed in the specification that were clearly intended to be covered by the claims.

There is no dispute that all of the sequences recited in the claims have either a valine at position 93 or at a position that corresponds to valine 93 of SEQ ID NO:89. Indeed, this is

demonstrated by the alignment of SEQ ID NOs. 83-108 in Appendix 12 of the Examiner's Answer. Furthermore, one of skill in the art could readily align the sequences to determine which valine residue corresponded to V93, as evidenced by the Examiner's submission of Appendix 12. Thus, to properly encompass mutants of all of the sequences recited in the claims, one of skill in the art would understand that the V93 mutation refers to a mutation at V93, if the sequence has a valine at position 93, or at a valine residue corresponding to V93 if the sequence does not have a valine at position 93. The Examiner's hyper-technical interpretation excludes certain embodiments from the claims and, thus, is inconsistent with what is described in the specification. *See Lisle Corp. v. A. J. Mfg. Co.*, 398 F.3d 1306, 1314, 73 USPQ2d 1891, 1895 (Fed. Cir. 2005) (rejecting accused infringer's "hyper-technical" literal construction of claim limitation reciting "said retainer being *detachably cooperative* with the tabs to rotate the disk and a tie rod engaged therewith," as requiring that tabs of wrench disk simultaneously detach from the retainer member while rotating a tie rod since that was an impossible mode of operation and not what was described in the specification).

CONCLUSION

For the reasons presented in the Appeal Brief filed 30 October 2008 and given above, pending claims 1-10 and 12-21 are allowable and reversal of the Examiner's rejection is respectfully requested.

To the extent any extension of time under 37 C.F.R. § 1.136 is required to obtain entry of this Reply Brief, such extension is hereby respectfully requested. If there are any fees due that are not enclosed, including any fees required for an extension of time under 37 C.F.R. § 1.136, please charge such fees to Deposit Account No. 50-3740.

Respectfully submitted,
Joseph A. SORGE et al.

Date: 8 September 2009

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Attachment: Copy of *Ex parte Anderson*, Appeal No. 2005-0908 (unpublished opinion).

ATTACHMENT

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte KIM VILBOUR ANDERSON, MARTIN SCHULEIN, LARS CHRISTIANSEN, BO DAMGAARD, and CLAUS VON DER OSTEN

Appeal No. 2005-0908
Application No. 09/261,329

ON BRIEF

Before WILLIAM F. SMITH, ADAMS, and GREEN, Administrative Patent Judges.

GREEN, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 204-206. Claim 204 is representative of the subject matter on appeal, and reads as follows:

204. A modified cellulase, comprising a substitution of the amino acid at position 119 with H in the amino acid of SEQ ID NO: 5, wherein each position is numbered according to the amino acid sequence of the cellulase of SEQ ID NO: 1 and the modified cellulase has endoglucanase activity.

The examiner relies upon no prior art.

Claims 204 and 206 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably covey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention, i.e., lack of adequate written description. Claims 204 and 206 also stand rejected under 35 U.S.C. § 112, first paragraph, on the grounds that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with the claims. Finally, claims 204-206 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that appellants regard as the invention. After careful review of the record and consideration of the issues before us, we reverse all of the rejections of record.

DISCUSSION

Claims 204 and 206 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably covey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention, i.e., lack of adequate written description.

According to the rejection, the use of "comprising" "allows for an undefined number of substitutions in addition to Q119H and reads on any structure that is not necessarily homologous with SEQ ID NO: 5." Examiner's Answer, page 3.

The examiner asserts further that "[t]he specification teaches the structure of only a single representative species of said genus, the modified endoglucanase from *Thielavia terrestris* having the sequence of SEQ ID NO:5 with the single substitution Q118H corresponding to the substitution Q119H in SEQ ID NO:1." Id. The genus encompassed by the claims, however, according to the examiner, "comprises variants additionally mutated at any of said 200 amino acid residues," and that "the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of being a modified cellulase having endoglucanase activity." Id. at 4. The examiner concludes "[g]iven this lack of description of representative species encompassed by the genus of claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention."

The burden is on the examiner to set forth a prima facie case of unpatentability. See In re Glaug, 283 F.3d 1335, 1338, 62 USPQ2d 1151, 1152 (Fed. Cir. 2002). The Court of Appeals for the Federal Circuit, our reviewing court, has addressed the issue of what constitutes adequate written description for claims drawn to a sequence. In Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1602 (Fed. Cir. 2002), the court adopted a portion of the

Guidelines proffered by the United States Patent and Trademark Office (USPTO). The court stated that:

> The written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of characteristics.

Enzo Biochem, 296 F.3d at 1324, 63 USPQ2d at 1613 (citations omitted).

As an initial matter, we would like to address the construction of claim 204. The claims recites "[a] modified cellulase, comprising a substitution of the amino acid at position 119 with H in the amino acid of SEQ ID NO: 5, wherein each position is numbered according to the amino acid sequence of the cellulase of SEQ ID NO: 1 and the modified cellulase has endoglucanase activity." We construe the claim as requiring starting with a cellulase of SEQ ID NO: 5, in which the amino acid at position 119 has been replaced with H, but also encompassing other modifications to the sequence, wherein the modifications may be substitutions, insertions or deletions, with the proviso that the resulting cellulose have endoglucanase activity.[1]

As to the merits of the rejection, Appellants argue that the specification provides "a precise definition by structure of the genus of modified cellulases sufficient to distinguish it from other modified cellulases" as well as "a description

of numerous representative members of the genus, in sufficient detail so that one of skill in the art would recognize that Applicants had invented the claimed subject matter." Appeal Brief, page 5. We agree, and the rejection is reversed.

First, as to function, the claims require that the cellulase have endoglucanase activity. The examiner does not argue, however, that the specification does not describe the functional characteristics or how to determine those characteristics.

Second, as to structure, the claims are drawn to a modified cellulase, wherein the parent cellulase is the cellulase of SEQ ID NO:5, and wherein the amino acid at position 119, wherein each position is numbered according to the cellulase of SEQ ID NO:1, is substituted with a histidine. The examiner contends that "[b]ecause 'comprising' is open language, and the claim allows for an undefined number of substitutions in addition to Q119H, [it thus] reads on any structure that is not necessarily homologous with SEQ ID NO: 5." Examiner's Answer, page 3. As noted above with respect to the construction of the claim, however, the claim requires that the skilled practitioner start with a cellulose having the sequence of SEQ ID NO: 5. Moreover, that statement ignores the limitation that the modified cellulose has endoglucanase activity—thus the claim sets forth complete or partial structure, i.e. SEQ ID NO. 5 coupled with disclosed

[1] We note also that the examiner required appellants to elect a single disclosed species for prosecution on the merits. See Paper No. 21. Appellants elected with traverse the cellulose of SEQ ID NO: 5, mutated at the position corresponding to position 119 in SEQ ID NO: 1. The rejections under 35 U.S.C. § 112, first paragraph, for lack of adequate written description and lack of enablement appear to be applicable to the genus, and not merely the elected species. Upon return of the application, the examiner should clarify the subject matter that has been examined, not only for purposes of 35 U.S.C. § 112, first paragraph, but also as to the prior art.

correlation with function, i.e., endoglucanase activity. See Enzo Biochem, 296 F.3d at 1324, 63 USPQ2d at 1613. The examiner argues further that the specification teaches the structure of only a single representative species of the genus encompassed by the claims, but, as noted by appellants, see Appeal Brief, page 5, the specification provides examples of mutations in tables 4-6 found at pages 28-35 of the specification. As the examiner has not supplied any evidence or reasoning why those mutations are not descriptive of the claimed modified cellulose, he has failed to meet his burden of establishing a prima facie case of unpatentability for lack of written description, and the rejection is reversed.

Claims 204 and 206 also stand rejected under 35 U.S.C. § 112, first paragraph, "because the specification, while being enabling for a modified cellulase having endoglucanase activity and the amino acid sequence of SEQ ID NO: 5 with a single substitution corresponding to a substitution Q119H in SEQ ID NO:1 (Q119H substitution), does not reasonably provide enablement for a modified cellulase having endoglucanase activity and an amino acid sequence comprising substitution Q119H and having an undefined percent identity to SEQ ID NO:5." Examiner's Answer, page 4.

According to the rejection, "[t]he state of the art does not allow the predictability of the properties based on the structure," nor does the "specification . . . teach which residues beside the specifically substituted are responsible for the resulting properties of the modified cellulase." Id. at 5. The examiner contends that as the amino acid sequence of a protein dictates its "structural and

functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired properties/activity requires a knowledge of guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of substitution and which are conserved (i.e. expectedly intolerant to substitution), and detailed knowledge of the ways in which the proteins' structure relates to its function." Id. at 5-6. But, the examiner asserts, the disclosure is limited to a single modified cellulase. See id. at 6.

The examiner further argues that "[w]hile recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions . . . and the positions within a protein's sequence where amino acid substitutions can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such substitutions is unpredictable." Id. (emphasis in original). Moreover, according to the rejection, the tolerance for substitutions decreases as the number of substitutions increases. See id.

The rejection concludes:

> The specification does not teach a rational and predictable scheme for substituting any residues in SEQ ID NO:5 with an expectation of obtaining the endoglucanase function that is exhibited by a disclosed mutant and the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.
>
> Therefore, on skilled in the art would require guidance beyond that provided in the specification as to how to make a modified cellulase having endoglucanase activity with the amino acid sequence of an unknown homology to SEQ ID NO:5. Without such guidance, the experimentation left to those skilled in the art is undue.

Id.

Appellants argue that the specification discloses a large number of modified cellulases and "illustrates how the cellulases are made and used." Appeal Brief, page 9. We agree.

"[A] specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971) (emphasis in original). "[It] is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." Id. at 224, 169 USPQ at 370.

The examiner argues that the specification teaches the structure of only a single representative species of the genus encompassed by the claims, but, as noted above, the specification provides examples of mutations in tables 4-6 found at pages 28-35 of the specification. The examiner does not supply any evidence or reasoning why the specification does not enable those disclosed mutations.

Moreover, the claims require that the modified enzyme have endglucanase activity. The examiner again does not provide any evidence that one skilled in the art would not be able to test for that activity. Here, the examiner has not provided "acceptable evidence or reasoning which is inconsistent" with the specification, and therefore has not met the initial burden of showing nonenablement, and the rejection is reversed.

Finally, claims 204-206 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that appellants regard as the invention.

According to the rejection:

> Claims 204-206 are drawn to a modified cellulase comprising a substitution Q199H "in the amino acid SEQ ID NO:5, wherein each position is numbered according to the amino acid sequence of the cellulase of SEQ ID NO:1". It is confusing to define a position number in one specific sequence (SEQ ID NO:5) using another sequence (SEQ ID NO:1) as opposed to the direct numbering the position in SEQ D NO:5. It is unclear what limitation is imposed on the scope of the claims by using said indirect numbering via SEQ ID NO:1. The specification discloses the alignment of SEQ ID NOs: 1 and 5 (pages 7-12, Table 1, columns 1 and 5, respectively). SEQ ID NO:1 has 202 amino acids whereas SEQ ID NO:5 has 201 amino acids. As shown in Table 1, SEQ ID NO:5 does not have an amino acid at the position corresponding to position 49 of SEQ ID NO:1. Thus, position Q118 in SEQ ID NO:5 corresponds to position Q119 in SEQ ID NO:1.

Examiner's Answer, page 7 (emphasis in original).

"The test for definiteness is whether one skilled in the art would understand the bounds of the claim when read in light of the specification." Miles Laboratories, Inc. v. Shandon, Inc., 997 F.2d 870, 875, 27 USPQ2d 1123, 1126 (Fed. Cir. 1993). Claims are in compliance with 35 U.S.C. § 112, second paragraph, if "the claims, read in light of the specification, reasonably apprise those skilled in the art and are as precise as the subject matter permits." Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1385, 231 USPQ 81, 94-95 (Fed. Cir. 1987).

Here, it is clear from the rejection that the examiner understands the bounds of the claim and understands which amino acid is being substituted. Moreover, as also noted by the examiner, the numbering system is explicitly set forth in Table 1 of the specification. Thus, one skilled in the art would understand the bounds of the claims, and the rejection is reversed.

The rejection further stated that "claim 206 is further confusing as reciting positions 21a, 49a, 49b, 95j and 150b. Neither SEQ ID NO: nor SEQ ID NOI:5 has these positions (Table 1)." Examiner's Answer, page 7.

We initially note that appears to be a new ground of rejection that was not designated as such, and as such, was improper. See 37 CFR § 41.39 (effective September 13, 2004). Be that as it may, however, we agree with appellants that

the lettering is adequately explained at page 6 and in Table 1 of the specification, see Reply Brief, page 1, and the rejection is reversed.

CONCLUSION

Because the examiner has failed to set forth a prima facie case of unpatentability under any of 35 U.S.C. § 112, first paragraph, written description, 35 U.S.C. § 112, first paragraph, scope of enablement, or 35 U.S.C. § 112, second paragraph, all of the rejections of record are reversed.

REVERSED

William F. Smith Administrative Patent Judge	)
Donald E. Adams Administrative Patent Judge	) BOARD OF PATENT) APPEALS AND) INTERFERENCES
Lora M. Green Administrative Patent Judge	)

LMG/jlb

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